Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) An imaging agent <u>suitable for diagnostic imaging in vivo</u> which comprises a metalloproteinase inhibitor of Formula (I) labelled with an imaging moiety <u>attached at the Y¹ or Y² positions</u>, wherein the imaging moiety can be detected following administration of said labelled matrix metalloproteinase inhibitor to the mammalian body *in vivo*:

where:

 Y^1 is H or -(CH₂)_w-(C=O)-Z; where w is an integer of value 1 to 6; and Z is OH, C_{1-6} alkoxy, C_{4-10} aryloxy or NR^1R^2 wherein R^1 and R^2 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} fluoroalkyl or C_{4-10} aryl.

 X^1 and X^2 together with the carbon atom to which they are attached, form a C_{3-10} saturated ring which may be alicyclic or bicyclic, and may optionally incorporate 1 or 2 heteroatoms chosen from O, N and S;

 X^3 is H, C_{1-3} alkyl or C_{1-3} fluoroalkyl;

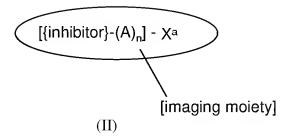
 Y^2 is a group of formula $-[A^1]_p[O]_qA^2$ where p and q are 0 or 1, and A^1 is C_{1-10} alkylene, C_{3-8} cycloalkylene, C_{1-10} perfluoroalkylene, C_{6-10} arylene or C_{2-10}

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heteroarylene, and A^2 is H, C_{1-10} alkyl, C_{3-8} cycloalkyl, C_{1-10} perfluoroalkyl, C_{6-10} aryl or C_{2-10} heteroaryl, with the proviso that when p=0, q is also 0 and A^2 is not H.

- 2. (Original) The imaging agent of Claim 1, where Y^1 is $-(CH_2)_w$ -(C=O)-Z and w is 1, 2 or 3.
- 3. (Withdrawn) The imaging agent of Claim 1, where X³ is H, CH₃ or CH₂F.
- 4. (Previously presented) The imaging agent of Claim 1 where Y^2 is $-C_6H_4$ -O-A², and A² is C_{6-10} aryl.
- 5. (Previously presented) The imaging agent of Claim 1, where the imaging moiety is chosen from:
 - (i) a radioactive metal ion;
 - (ii) a paramagnetic metal ion;
 - (iii) a gamma-emitting radioactive halogen;
 - (iv) a positron-emitting radioactive non-metal;
 - (v) a hyperpolarised NMR-active nucleus;
 - (vi) a reporter suitable for *in vivo* optical imaging;
 - (vii) a β-emitter suitable for intravascular detection.
- 6. (Previously presented) The imaging agent of Claim 1, where the imaging agent is of Formula II:



where:

{inhibitor} is the metalloproteinase inhibitor of Formula (I);

-(A)_n- is a linker group wherein each A is independently -CR₂- , -CR=CR- , -C \equiv C- , -CR₂CO₂- , -CO₂CR₂- , -NRCO- , -CONR- , -NR(C \equiv O)NR-, -NR(C \equiv S)NR-, -SO₂NR- , -NRSO₂- , -CR₂OCR₂- , -CR₂SCR₂- , -CR₂NRCR₂- , a C₄₋₈ cycloheteroalkylene group, a C₄₋₈ cycloalkylene group, a C₅₋₁₂ arylene group, or a C₃₋₁₂ heteroarylene group, an amino acid, a sugar or a monodisperse polyethyleneglycol (PEG) building block;

R is independently chosen from H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxyalkyl or C_{1-4} hydroxyalkyl; n is an integer of value 0 to 10; and and X^a is H, OH, Hal, NH₂, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxyalkyl or X^a is the imaging moiety.

- 7. (Withdrawn) The imaging agent of Claim 6, where the imaging moiety is attached at the Y^1 or Y^2 positions of the metalloproteinase inhibitor.
- 8. (Previously presented) The imaging agent of Claim 1, where the matrix metalloproteinase inhibitor is conjugated to a ligand, and said ligand forms a metal complex with an imaging moiety which is a radioactive metal ion or paramagnetic metal ion as defined in options (i) and (ii) of claim 5.
- 9. (Original) The imaging agent of Claim 8, where the ligand is a chelating agent.
- 10. (Previously presented) The imaging agent of Claim 8, where the radioactive metal ion is a gamma emitter or a positron emitter.
- 11. (Withdrawn) The imaging agent of Claim 10, where the radioactive metal ion is ^{99m}Tc, ¹¹¹In, ⁶⁴Cu, ⁶⁷Cu, ⁶⁷Ga or ⁶⁸Ga.

- 12. (Currently amended) The imaging agent of Claim $\underline{510}$, where the gamma-emitting radioactive halogen imaging moiety is 123 I.
- 13. (Withdrawn) The imaging agent of Claim 10, where the positron-emitting radioactive non-metal is chosen from ¹⁸F, ¹¹C or ¹³N.
- 14. (Withdrawn) The imaging agent of Claim 1, where the matrix metalloproteinase inhibitor is of Formula IV:

$$(CH_2)_w(CO)Z$$
 X^3O
 N
 CH_2
 CH_2

where: Y², w and Z are as defined in Claim 1;

X³ is H, CH₃ or CH₂F;

 X^4 is –(CH₂)_m- where m is 1, 2 or 3, -CH₂OCH₂- or X^5 where X^5 is

where t is 2 or 3.

15. (Withdrawn) The imaging agent of Claim 14, where Z is NR¹R².

16. (Previously presented) The imaging agent of Claim 1, where the matrix metalloproteinase inhibitor is of Formula V:

$$(CH_2)_w(CO)Z$$

$$HO \bigvee_{CH_2 \ CH_2 \ O} \bigvee_{CH_2 \ CH_2 \ O} \bigvee_{(V)} \bigvee_{(V)}$$

where:

 X^6 is Hal, R^1 or OR^1 , where R^1 is C_{1-3} alkyl or C_{1-3} fluoroalkyl.

- 17. (Original) The imaging agent of Claim 16, where Z is NR^1R^2 , X^6 is F; and X^4 is $-(CH_2)_2$ -, $-CH_2OCH_2$ or X^5 with t equal to 2.
- 18. (Previously presented) A pharmaceutical composition which comprises the imaging agent of Claim 1 together with a biocompatible carrier, in a form suitable for mammalian administration.
- 19. (Previously presented) A radiopharmaceutical composition which comprises the imaging agent of Claim 1 where the imaging moiety is radioactive, together with a biocompatible carrier, in a form suitable for mammalian administration.
- 20. (Original) The radiopharmaceutical composition of claim 19, where the imaging moiety comprises a radioactive metal ion.
- 21. (Original) The radiopharmaceutical composition of claim 19, where the imaging moiety comprises a positron-emitting radioactive non-metal or a gamma-emitting radioactive halogen.

- 22. (Previously presented) A conjugate of a matrix metalloproteinase inhibitor of Formula (I) as defined in Claim 1 with a ligand, wherein said ligand is capable of forming a metal complex with an imaging moiety which is a radioactive or paramagnetic metal ion <u>as</u> defined in options (i) and (ii) of claim 5.
- 23. (Previously presented) The conjugate of Claim 22, of Formula IIb:

where {inhibitor}, A and n are as defined in Claim 6; and X^b is H, OH, Hal, NH₂, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxyalkyl, C_{1-4} hydroxyalkyl or X^b is the ligand.

24. (Previously presented) The conjugate of Claim 22, wherein the matrix metalloproteinase inhibitor is of Formulae IV

where: Y², w and Z are as defined in Claim 1;

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 X^3 is H, CH₃ or CH₂F;

 X^4 is $-(CH_2)_{m^-}$ where m is 1, 2 or 3, $-CH_2OCH_2$ - or X^5 where X^5 is

where t is 2 or 3 or wherein the matrix metalloproteinase inhibitor is of Formulae V

$$(CH_2)_w(CO)Z$$

$$HO \bigvee_{N} \bigvee_{CH_2 \ CH_2 \ O} \bigvee_{O} \bigvee_{(V)} \bigvee$$

where:

 X^6 is Hal, R^1 or OR^1 , where R^1 is C_{1-3} alkyl or C_{1-3} fluoroalkyl.

- 25. (Previously presented) The conjugate of Claim 22, wherein the ligand is a chelating agent.
- 26. (Original) The conjugate of Claim 25, wherein the chelating agent has a diaminedioxime, N_2S_2 , or N_3S donor set.
- 27. (Previously presented) A kit for the preparation of the radiopharmaceutical composition of Claim 20.

- 28. (Currently amended) The kit of Claim <u>2730</u>, where the radioactive metal ion is ^{99m}Tc, and the kit further comprises a biocompatible reductant.
- 29. (Previously presented) A kit for the preparation of the radiopharmaceutical composition of Claim 21, which comprises a precursor, said precursor being a non-radioactive derivative of the matrix metalloproteinase inhibitor of wherein said non-radioactive derivative is capable of reaction with a source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen to give the desired radiopharmaceutical.
- 30. (Original) The kit of claim 29 where the precursor is in sterile, apyrogenic form.
- 31. (Previously presented) The kit of Claim 29, where the source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen is chosen from:
 - (i) halide ion or F^+ or I^+ ; or
 - (ii) an alkylating agent chosen from an alkyl or fluoroalkyl halide, tosylate, triflate or mesylate.
- 32. (Withdrawn) The kit of Claim 29, where the non-radioactive derivative is chosen from:
 - (i) an organometallic derivative such as a trialkylstannane or a trialkylsilane;
 - (ii) a derivative containing an alkyl halide, alkyl tosylate or alkyl mesylate for nucleophilic substitution;
 - (iii) a derivative containing an aromatic ring activated towards nucleophilic or electrophilic substitution;
 - (iv) a derivative containing a functional group which undergoes facile alkylation;
 - (v) a derivative which alkylates thiol-containing compounds to give a thioethercontaining product.
- 33. (Previously presented) The kit of Claim 29, where the precursor is bound to a solid phase.

- 34. (Withdrawn) A method of diagnostic imaging of atherosclerosis of a mammalian subject *in vivo*, which comprises administration of the imaging agent of Claim 1 to said subject, followed by detection of the imaging moiety of said imaging agent.
- 35. (Withdrawn) A method of diagnostic imaging of unstable plaques of a mammalian subject *in vivo*, which comprises administration of the imaging agent of Claim 1 to said subject, followed by detection of the imaging moiety of said imaging agent.
- 36. (Withdrawn) A method of intravascular detection of atherosclerosis of a mammalian subject *in vivo*, which comprises administration of the imaging agent of Claim 1 to said subject, followed by detection of the imaging moiety of said imaging agent.